

Amendment

1. (currently amended) A milnacipran formulation that provides delayed or extended release of milnacipran to produce a therapeutic effect over approximately 24 hours when administered to a patient in need, with diminished incidence ~~and~~ or reduced intensity relative to one or more immediate release milnacipran side effects.

2. (original) The milnacipran formulation according to Claim 1, wherein the side effect is nausea.

3. (currently amended) The ~~milnacipran~~ milnacipran formulation according to Claim 1, wherein the side effects are selected from the group consisting of vomiting, headache, tremulousness, anxiety, panic attacks, palpitations, urinary retention, orthostatic hypotension, diaphoresis, chest pain, rash, weight gain, back pain, constipation, vertigo, increased sweating, agitation, hot flushes, tremors, fatigue, somnolence, dyspepsia, dysoria, nervousness, dry mouth, abdominal pain, irritability, and insomnia.

4. (original) The milnacipran formulation according to Claim 1 having a milnacipran release profile that is characterized by release of less than approximately 10% of the total dose over a period up to four hours, followed by a slow or extended drug release.

5. (original) The milnacipran formulation according to Claim 4 wherein the defined period of time is between approximately four and approximately twenty-four hours.

AMENDMENT AND RESPONSE TO OFFICE ACTION

6. (original) The milnacipran formulation according to Claim 1 providing milnacipran blood plasma levels that are characterized by T_{\max} at 4-10 hours, and C_{\max} below approximately 3000 ng/ml.

7. (original) The milnacipran formulation according to Claim 6 providing milnacipran blood plasma levels that are characterized by C_{\max} below approximately 2000 ng/ml.

8. (original) The milnacipran formulation according to Claim 6 providing milnacipran blood plasma levels that are characterized by C_{\max} below approximately 1000 ng/ml.

9. (original) The milnacipran formulation according to Claim 1 further comprising at least one other active compound selected from the group consisting of analgesics, anti-inflammatory drugs, antipyretics, antidepressants, antiepileptics, antihistamines, antimigraine drugs, antimuscarinics, anxiolytics, sedatives, hypnotics, antipsychotics, bronchodilators, anti asthma drugs, cardiovascular drugs, corticosteroids, dopaminergics, electrolytes, gastro-intestinal drugs, muscle relaxants, nutritional agents, vitamins, parasymphathomimetics, stimulants, anorectics, and anti-narcoleptics.

10. (original) The milnacipran formulation according to Claim 9 comprising compounds selected from the group consisting of aceclofenac, acetaminophen, adomoxetine, almotriptan, alprazolam, amantadine, amcinonide, aminocyclopropane, amitriptyline, amolodipine, amoxapine, amphetamine, aripiprazole, aspirin, atomoxetine, azasetron, azatadine, beclomethasone, benactyzine, benoxaprofen, bermoprofen, betamethasone, bicifadine,

AMENDMENT AND RESPONSE TO OFFICE ACTION

bromocriptine, budesonide, buprenorphine, bupropion, buspirone, butorphanol, butriptyline, caffeine, carbamazepine, carbidopa, carisoprodol, celecoxib, chlordiazepoxide, chlorpromazine, choline salicylate, citalopram, clomipramine, clonazepam, clonidine, clonitazene, clorazepate, clotiazepam, cloxazolam, clozapine, codeine, corticosterone, cortisone, cyclobenzaprine, cyproheptadine, demexiptiline, desipramine, desomorphine, dexamethasone, dexanabinol, dextroamphetamine sulfate, dextromoramide, dextropropoxyphene, dezocine, diazepam, dibenzepin, diclofenac sodium, diflunisal, dihydrocodeine, dihydroergotamine, dihydromorphine, dimetacrine, divalproex, dizatriptan, dolasetron, donepezil, dothiepin, doxepin, duloxetine, ergotamine, escitalopram, estazolam, ethosuximide, etodolac, femoxetine, fenamates, fenoprofen, fentanyl, fludiazepam, fluoxetine, fluphenazine, flurazepam, flurbiprofen, flutazolam, fluvoxamine, frovatriptan, gabapentin, galantamine, gepirone, ginko bilboa, granisetron, haloperidol, huperzine A, hydrocodone, hydrocortisone, hydromorphone, hydroxyzine, ibuprofen, imipramine, indiplon, indomethacin, indoprofen, iprindole, ipsapirone, ketaserin, ketoprofen, ketorolac, lesopitron, levodopa, lipase, lofepramine, lorazepam, loxapine, maprotiline, mazindol, mefenamic acid, melatonin, melitracen, memantine, meperidine, meprobamate, mesalamine, metapramine, metaxalone, methadone, methadone, methamphetamine, methocarbamol, methylodopa, methylphenidate, methylsalicylate, methysergid(e), metoclopramide, mianserin, mifepristone, milnacipran, minaprine, mirtazapine, moclobemide, modafinil, molindone, morphine, morphine hydrochloride, nabumetone, nadolol, naproxen, naratriptan, nefazodone, neurontin, nomifensine, nortriptyline, olanzapine, olsalazine, ondansetron, opipramol, orphenadrine, oxaflozane, oxaprazin, oxazepam, oxitriptan, oxycodone,

AMENDMENT AND RESPONSE TO OFFICE ACTION

oxymorphone, pancrelipase, parecoxib, paroxetine, pemoline, pentazocine, pepsin, perphenazine, phenacetin, phendimetrazine, phenmetrazine, phenylbutazone, phenytoin, phosphatidylserine, pimozone, pirlindole, piroxicam, pizotifen, pizotyline, pramipexole, prednisolone, prednisone, pregabalin, propranolol, propizipine, propoxyphene, protriptyline, quazepam, quinupramine, reboxetine, reserpine, risperidone, ritanserine, rivastigmine, rizatriptan, rofecoxib, ropinirole, rotigotine, salsalate, sertraline, sibutramine, sildenafil, sulfasalazine, sulindac, sumatriptan, tacrine, temazepam, tetrabenazine, thiazides, thioridazine, thiothixene, tiapride, tiaspirone, tizanidine, tofenacin, tolmetin, tolaxatone, topiramate, tramadol, trazodone, triazolam, trifluoperazine, trimethobenzamide, trimipramine, tropisetron, valdecoxib, valproic acid, venlafaxine, viloxazine, vitamin E, zimeldine, ziprasidone, zolmitriptan, zolpidem, zopiclone and isomers, salts, and combinations thereof.

11. (original) The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of dextrogyral or levogyral enantiomers of the milnacipran or pharmaceutically acceptable salts thereof.

12. (original) The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of a mixture of milnacipran enantiomers or pharmaceutically acceptable salts thereof.

13. (original) The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of the active metabolite of milnacipran or pharmaceutically acceptable salts thereof.

AMENDMENT AND RESPONSE TO OFFICE ACTION

14. (original) The milnacipran formulation according to Claim 1, wherein the milnacipran is in the form of a therapeutically equivalent dose of para-hydroxy-milnacipran (F2782) or pharmaceutically acceptable salts thereof.

15. (original) The milnacipran formulation according to Claim 1 comprising an enteric coating.

16. (original) The milnacipran formulation according to Claim 1, wherein the administrable milnacipran unit dose is from 25 to 500 mg.

17. (original) The milnacipran formulation according to Claim 1, wherein the administrable milnacipran unit dose is from 200 to 500 mg.

18. (original) The formulation according to Claim 9 comprising 25 to 500 mg milnacipran and 100 to 600 mg modafinil.

19. (original) A milnacipran formulation that allows extended release of a therapeutically effective amount of milnacipran over approximately 24 hours when administered to a patient in need, comprising

an extended-release milnacipran formulation coated with an enteric coating, wherein the enteric coated formulation remains intact or substantially intact in the stomach but dissolves and releases the contents of the dosage form once it reaches the small intestine, over a period of time resulting in therapeutic milnacipran blood plasma levels for an extended period of time before returning to the steady-state level at night time to avoid sleep disturbances.

20. (original) A kit comprising the milnacipran formulation of Claim 1.

AMENDMENT AND RESPONSE TO OFFICE ACTION

21. (original) The kit of Claim 20 comprising different dosage units of milnacipran to allow for dosage escalation.

22. (original) The kit of Claim 20 comprising instruction on taking the formulation once daily before bedtime.

23. (canceled)

24. (canceled)